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<120> MODIFICATIONS OF THE VEGF RECEPTOR-2 PROTEIN AND METHODS OF USE

<130> 0125-0016US

<140> 09/390,326

<141> 1999-09-07

<160> 12

<170> PatentIn Ver. 2.0

<210> 1

<211> 31

<212> DNA

<213> Homo sapiens

<400> 1

cagcatatgg atccagatga actcccattg q

<210> 2

<211> 34

<212> DNA

<213> Homo sapiens

<400> 2

gcggtcgact taaacaggag gagagctcag tgtg

<210> 3

<211> 33

<212> DNA

<213> Homo sapiens

<400> 3

gcacatatgg aacgactgcc ttatgatgcc agc

<210> 4

<211> 38

<212> DNA

<213> Homo sapiens

<400> 4

cctgtcgact tatccagaat cctcttccat gctcaaag

38

31

34

33

<210> 5

<211> 317

<212> PRT

<213> Homo sapiens

<400> 5

Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His Cys Glu Arg Leu Pro

1 5 10 15

Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp Arg Leu Lys Leu Gly
20 25 30

Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala
35 40 45

Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr Val Ala Val Lys Met 50 55 60

Leu Lys Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu
65 70 75 80

Leu Lys Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu 85 90 95

Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu
100 105 110

Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Ser Lys Arg Asn 115 120 125

Glu Phe Val Pro Tyr Lys Glu Ala Pro Glu Asp Leu Tyr Lys Asp Phe 130 135 140

Leu Thr Leu Glu His Leu Leu Ile Cys Tyr Ser Phe Gln Val Ala Lys 145 150 155 160

Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala 165 170 175

Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile Cys Asp 180 185 190

Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys
195 200 205

Gly Asp Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Thr Ile Phe 210 220

Asp Arg Val Tyr Thr Ile Gln Ser Asp Val Trp Ser Phe Gly Val Leu 230 235 240

Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Lys 245 250 255

Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg Met Arg 260 265 270

Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu Asp Cys 275 280 285

Trp His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu Val Glu 290 295 300

His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp 305 310 315

<210> 6

<211> 386

<212> PRT

<213> E. coli

<400> 6

Asp Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp
1 5 10 15

Gly Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val 20 25 30

Val Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys
35 40 45

Val Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln 50 60

Ala Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu 65 70 75 80

Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr 85 90 95

Ile Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His
100 105 110

Lys Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys
115 120 125

Glu Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser 130 135 140

Tyr Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys
145 150 155 160

Gln Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val 165 170 175

Ser Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser 180 185 190

Tyr Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser 195 200 205

Asp Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr 210 215 220

Tyr Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val 225 230 235 240

His Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile 245 250 255

Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser 260 265 270

Asn Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala 275 280 285

Pro Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp 290 295 300

Ser Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro 305 310 315 320

Tyr Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser 325 330 335

Gly Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu 340 345 350

Ile Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe 355 360 365

Tyr His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys 370 380

Lys Ser 385

<210> 7

<211> 310

<212> PRT

<213> Homo sapiens

<400> 7

Met Leu Ala Gly Val Ser Glu Tyr Glu Leu Pro Glu Asp Pro Arg Trp
1 5 10 15

Glu Leu Pro Arg Asp Arg Leu Val Leu Gly Lys Pro Leu Gly Glu Gly
20 25 30

Cys Phe Gly Gln Val Val Leu Ala Glu Ala Ile Gly Leu Asp Lys Asp 35 40 45

Lys Pro Asn Arg Val Thr Lys Val Ala Val Lys Met Leu Lys Ser Asp 50 55 60

Ala Thr Glu Lys Asp Leu Ser Asp Leu Ile Ser Glu Met Glu Met 65 . 70 75 80

Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys
85 90 95

Thr Gln Asp Gly Pro Leu Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly
100 105 110

Asn Leu Arg Glu Tyr Leu Gln Ala Arg Arg Pro Pro Gly Leu Glu Tyr
115 120 / 125

Cys Tyr Asn Pro Ser His Asn Pro Glu Glu Gln Leu Ser Ser Lys Asp 130 135 140

Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu Ala 145 150 155 160

Ser Lys Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu Val 165 170 175

Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp 180 185 190

Ile His His Ile Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro
195 200 205

Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Ile Tyr Thr His 210 215 220

Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Thr 225 235 235

Leu Gly Gly Ser Pro Tyr Pro Gly Val Pro Val Glu Glu Leu Phe Lys 245 250 255

Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ser Asn Cys Thr Asn 260 265 270

Glu Leu Tyr Met Met Met Arg Asp Cys Trp His Ala Val Pro Ser Gln 275 280 285

Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Ile Val Ala 290 295 300

Leu Thr Ser Asn Gln Glu 305 310

<210> 8

<211> 297

<212> PRT

<213> Homo sapiens

<400> 8

Val Phe Pro Cys Ser Val Tyr Val Pro Asp Glu Trp Glu Val Ser Arg

1 5 10 15

Glu Lys Ile Thr Leu Leu Arg Glu Leu Gly Gln Gly Ser Phe Gly Met

Val Tyr Glu Gly Asn Ala Arg Asp Ile Ile Lys Gly Glu Ala Glu Thr
35 40 45

Arg Val Ala Val Lys Thr Val Asn Glu Ser Ala Ser Leu Arg Glu Arg 50 55 60

Ile Glu Phe Leu Asn Glu Ala Ser Val Met Lys Gly Phe Thr Cys His
65 70 75 80

His Val Val Arg Leu Leu Gly Val Val Ser Lys Gly Gln Pro Thr Leu 85 90 95

Val Val Met Glu Leu Met Ala His Gly Asp Leu Lys Ser Tyr Leu Arg

Ser Leu Arg Pro Glu Ala Glu Asn Asn Pro Gly Arg Pro Pro Pro Thr 115 120 125

Leu Gln Glu Met Ile Gln Met Ala Ala Glu Ile Ala Asp Gly Met Ala 130 135 140

Cys Met Val Ala His Asp Phe Thr Val Lys Ile Gly Asp Phe Gly Met 165 170 175

Thr Arg Asp Ile Tyr Glu Thr Asp Tyr Tyr Arg Lys Gly Gly Lys Gly 180 185 190

Leu Leu Pro Val Arg Trp Met Ala Pro Glu Ser Leu Lys Asp Gly Val

Phe Thr Thr Ser Ser Asp Met Trp Ser Phe Gly Val Val Leu Trp Glu 210 215 220

Ile Thr Ser Leu Ala Glu Gln Pro Tyr Gln Gly Leu Ser Asn Glu Gln 225 230 235 240

Val Leu Lys Phe Val Met Asp Gly Gly Tyr Leu Asp Gln Pro Asp Asn 245 250 255

Cys Pro Glu Arg Val Thr Asp Leu Met Arg Met Cys Trp Gln Phe Asn 260 265 270

Pro Asn Met Arg Pro Thr Phe Leu Glu Ile Val Asn Leu Leu Lys Asp 275 280 285

Asp Leu His Pro Ser Phe Pro Glu Val 290 295

<210> 9

<211> 367 ·

<212> PRT

<213> Homo sapiens

<400> 9

Met Asp Pro Asp Glu Val Pro Leu Asp Glu Gln Cys Glu Arg Leu Pro

1 5 10 15

Tyr Asp Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg Leu Lys Leu Gly Lys Ser Leu Gly Arg Gly Ala Phe Gly Lys Val Val Gln Ala Ser Ala Phe Gly Ile Lys Lys Ser Pro Thr Cys Arg Thr Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala Leu Met Thr Glu Leu Lys Ile Leu Thr His Ile Gly His His Leu Asn Val Val Asn Leu 90 Leu Gly Ala Cys Thr Lys Gln Gly Gly Pro Leu Met Val Ile Val Glu 105 Tyr Cys Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys Ser Lys Arg Asp 120 Leu Phe Phe Leu Asn Lys Asp Ala Ala Leu His Met Glu Pro Lys Lys 130 Glu Lys Met Glu Pro Gly Leu Glu Gln Gly Lys Lys Pro Arg Leu Asp 155 Ser Val Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly Phe Gln Glu Asp 165

Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Asp Ser Asp Gly Phe Tyr 180 185 190

Lys Glu Pro Ile Thr Met Glu Asp Leu Ile Ser Tyr Ser Phe Gln Val 195 200 205

Ala Arg Gly Met Glu Phe Leu Ser Ser Arg Lys Cys Ile His Arg Asp 210 215 220

Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Asn Asn Val Val Lys Ile 225 230 235 240

Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asn Pro Asp Tyr Val 245 250 255

Arg Lys Gly Asp Thr Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser 260 265 270

Ile Phe Asp Lys Ile Tyr Ser Thr Lys Ser Asp Val Trp Ser Tyr Gly
275 280 285

Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Ser Pro Tyr Pro Gly 290 295 300

Val Gln Met Asp Glu Asp Phe Cys Ser Arg Leu Arg Glu Gly Met Arg 305 310 315 320

30

Met Arg Ala Pro Glu Tyr Ser Thr Pro Glu Ile Tyr Gln Ile Met Leu 330 Asp Cys Trp His Arg Asp Pro Lys Glu Arg Pro Arg Phe Ala Glu Leu 345 Val Glu Lys Leu Gly Asp Leu Leu Gln Ala Asn Val Gln Gln Asp 360 <210> 10 <211> 30 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Oligonucleotide <400> 10 ctcagcagga ttgataagac tacattgttc <210> 11 <211> 36 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Oligonucleotide <400> 11 gaatttgtcc cctacaagga agctcctgaa gatctg 36 <210> 12 <211> 367 <212> PRT <213> Homo sapiens <400> 12 Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His Cys Glu Arg Leu Pro 10 Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp Arg Leu Lys Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu

Leu Lys Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu

90

Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu 105 Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Ser Lys Arg Asn 120 Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg Phe Arg Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly Phé Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro Glu Asp Leu Tyr Lys 185 Asp Phe Leu Thr Leu Glu His Leu Leu Ile Cys Tyr Ser Phe Gln Val 200 Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly Asp Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Thr Ile Phe Asp Arg Val Tyr Thr Ile Gln Ser Asp Val Trp Ser Phe Gly 280

Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly

Val Lys Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg

Met Arg Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu 325

Asp Cys Trp His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu 340 345 350

Val Glu His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp 355 360 365